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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/594,014

09/25/2006

Petrus Jacobus Dekker

GRT/4662-335

3949

23117 7590 12/24/2009
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EXAMINER

PAK, YONG D

ART UNIT

PAPER NUMBER

1652

MAIL DATE

DELIVERY MODE

12/24/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/594,014	Applicant(s) DEKKER ET AL.	
	Examiner YONG D. PAK	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 September 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10, 12-23 and 26-38 is/are pending in the application.
- 4a) Of the above claim(s) 22, 23, 37 and 38 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10, 12-21, and 26-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This application is a 371 of PCT/JP05/04392.

The amendment filed September 21, 2009, canceling claims 1-9, 11, and 24-25, amending claims 10 and 15-23, and adding claims 26-38, has been entered.

Claims 10, 12-23, and 26-38 are pending. Claims 22-23 and 37-38 are withdrawn. Claims 10, 12-21, and 26-36 are under consideration.

Election/Restrictions

Newly submitted claims 37-38 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claims 37-38 are drawn to a method of using the elected product.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 37-38 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Response to Arguments

Applicant's amendment and arguments filed on September 21, 2009, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

In view of the amendment of claims 18 and 21, the objections to claims 18 and 21 have been **withdrawn**.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10, 12-21, and 26-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 10, 12-21, and 26-36 are drawn to a mutant filamentous fungus, *Aspergillus*, *Penicillium*, *Trichoderma*, *Aspergillus niger*, *Aspergillus oryzae*, *Penicillium chrysogenum*, or *Penicillium citrinum* cell having a preference for NHR and having a decreased ratio of NHR/HR as compared to the wildtype of said cell or increased frequency of targeted integration of a polynucleotide to a predetermined genomic site, wherein said mutant **(A)** is deficient in a gene encoding a component involved in NHR, has a decreased level of a component involved in NHR, gene involved in NHR has been replaced by a non-functional variant, or has an increased level of a component involved in HR, or **(B)** is deficient in its hdfA, hdfB, and/or homologues thereof, and a method of

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using said cell to produce a polypeptide of interest. Therefore, these claims encompass any all mutant filamentous fungus, any or all mutant *Aspergillus*, any or all mutant *Penicillium*, any or all mutant *Trichoderma*, *Aspergillus niger*, *Aspergillus oryzae*, *Penicillium chrysogenum*, or *Penicillium citrinum* cell having a preference for NHR and having a decreased ratio of NHR/HR as compared to the wildtype of said cell or increased frequency of targeted integration of a polynucleotide to a predetermined genomic site, wherein said mutant **(A)** is deficient in any gene encoding any or all component involved in NHR, has a decreased level of any or all component involved in NHR, or any gene involved in NHR replaced by any non-functional variant, **(B)** is deficient in *hdfA*, *hdfB*, and/or any homologues thereof, and **(C)** has an increased level of any or all component involved in HR and a method of using said cell to produce a polypeptide of interest. Therefore, these claims are drawn to a genus of any or all mutant filamentous fungus, any or all mutant *Aspergillus*, any or all mutant *Penicillium*, any or all mutant *Trichoderma*, *Aspergillus niger*, *Aspergillus oryzae*, *Penicillium chrysogenum*, or *Penicillium citrinum* comprising **(A)** deletion/mutation of any gene involved in NHR, **(B)** deletion of *hdfA*, *hdfB* or homologues thereof and **(C)** an increased level of any component involved in HR, wherein said mutant cell has a decreased ratio of NHR/HR as compared to the wildtype of said cell. The specification describes a mutant *Aspergillus niger* and *Penicillium chrysogenum* comprising a deletion of its *hdfA* and/or *hdfB* genes, wherein said cells have a decreased ratio of NHR/HR as compared to the wildtype of said cell. However, the specification does not provide an actual reduction to practice of the claimed filamentous fungus, *Aspergillus*, *Penicillium*,

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Trichoderma, *Aspergillus oryzae*, or *Penicillium citrinum* cells because the specification fails to disclose the structure of *hdfA* and *hdfB* (or their homologs) genes in non-*Aspergillus niger* and *Penicillium chrysogenum* which must be known in order to delete/mutate said genes in the claimed filamentous fungal, *Aspergillus*, *Penicillium*, *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* cells, which comprises any or all filamentous fungus, any or all *Aspergillus*, any or all *Penicillium*, any or all *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum*, wherein its *hdfA* or *hdfB* or homologs thereof are mutated or deleted. The specification does not disclose the isolation or cloning of any non-*A. niger* and non-*P. chrysogenum* *hdfA* or *hdfB* genes. The specification does not describe any structural features of non-*A. niger* and non-*P. chrysogenum* *hdfA* or *hdfB* genes that would have been expected to be shared by other yeast or other filamentous fungus, *Aspergillus*, *Penicillium*, *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* cells *hdfA* or *hdfB* (or homologs thereof) genes. The specification also does not describe any structural features of the claimed genus of filamentous fungus comprising an increased level of a component involved in HR. The level of knowledge and skill in the art does not allow those skilled in the art to structurally envisage or recognize any or all filamentous fungus, any or all *Aspergillus*, any or all *Penicillium*, any or all *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* having a deletion or mutation of its *hdfA*, *hdfB* or homologs thereof or increased level of a component involved in HR because it is known that corresponding genes in different species tend to differ in sequence and the amount and type of sequence variation is unpredictable. Since the structure of *hdfA*, *hdfB* and homologs thereof would be

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expected to vary unpredictable from the structure of the *A. niger* and *P. chrysogenum* *hdfA* and *hdfB*, the disclosed *A. niger* and *P. chrysogenum* mutants comprising a deletion of its *hdfA* and *hdfB* do not constitute a representative number of species to describe the whole genus of any or all filamentous fungus, any or all *Aspergillus*, any or all *Penicillium*, any or all *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* comprising a mutated or deleted *hdfA*, *hdfB* and/or homologs thereof and there is no evidence on the record of the relationship between the structure of the disclosed mutant *A. niger* or *P. chrysogenum* and the structure of any or all filamentous fungus, any or all *Aspergillus*, any or all *Penicillium*, any or all *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* comprising a deletion or mutation of its *hdfA*, *hdfB* and/or homologs thereof. Because the disclosed *A. niger* and *P. chrysogenum* mutant having a deletion of its *hdfA* and *hdfB* are not representative of the entire claimed genus, and the specification does not disclose structural features shared by members of the genus, the description of the said mutant *A. niger* and *P. chrysogenum* having a deletion of its *hdfA* and *hdfB* would not have put the application in possession of the common structural attributes or features shared by members of the genus that structurally distinguish the members of the genus from other materials at the time of filing. Thus, the description of the *A. niger* and *P. chrysogenum* mutant having a deletion of its *hdfA* and *hdfB* is not sufficient to describe the claimed genus of any or all filamentous fungus, any or all *Aspergillus*, any or all *Penicillium*, any or all *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* comprising a deletion or mutation of its *hdfA*, *hdfB* and/or homologs thereof. Accordingly, the specification does not provide a representative number of

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species or sufficient common structural features to show that the application would have been in possession of the claimed genus as a whole at the time of filing. Therefore, the specification fails to describe a representative species of the genus comprising any or all filamentous fungus, any or all *Aspergillus*, any or all *Penicillium*, any or all *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* comprising a deletion or mutation of its *hdfA*, *hdfB* and/or homologs thereof.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 10, 12-21, and 26-36.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that the claims meet the written description requirement because (1) the specification on pages 1-2 discusses the high level of skill and knowledge in the prior art, such as *Saccharomyces* mutants that are deficient in a gene involved in non-homologous recombination, (2) the specification discloses two filamentous fungi mutants, *Aspergillus niger* and *Penicillium chrysogenum*, wherein said mutants have been steered towards HR by deletion of its *hdfA/hdfB* genes, and (3) as

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of the effective filing date of the present invention, a plethora of genomes of filamentous fungi were known and homologues of KU70, KU80 and other genes involved in NHR.

Examiner respectfully disagrees. The claims are drawn to mutants of any or all filamentous fungi, wherein it's hdfA/hdfB/KU70/KU80 homologs have been inactivated, resulting in increased HR. Knowledge of *Saccharomyces* KU70 gene or other non-filamentous fungi hdfA/hdfB/KU70/KU80 gene homologs and mutants lacking said genes is not representative of the entire claimed genus since the genes of any filamentous fungal hdfA/hdfB/KU70/KU80 homologs must be known in order to inactivate said genes in any filamentous fungi to arrive at the claimed mutant filamentous fungi. However, the specification only describes two species, a mutant *Aspergillus niger* and *Penicillium chrysogenum* comprising a deletion of its hdfA and/or hdfB genes, wherein said fungi have a decreased ratio of NHR/HR as compared to the wildtype of said fungi. Therefore, the specification does not provide an actual reduction to practice of the claimed filamentous fungus, *Aspergillus*, *Penicillium*, *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* cells because the specification fails to disclose the structure of hdfA and hdfB (or their homologs) genes in non- *Aspergillus niger* and *Penicillium chrysogenum* filamentous fungi which must be known in order to delete/mutate said genes in the claimed filamentous fungal. The specification does not disclose the isolation or cloning of any non-*A. niger* and non-*P. chrysogenum* hdfA or hdfB genes. The specification does not describe any structural features of non-*A. niger* and non-*P. chrysogenum* hdfA or hdfB genes that would have been expected to be shared by other yeast or other filamentous fungus, *Aspergillus*, *Penicillium*,

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Trichoderma, *Aspergillus oryzae*, or *Penicillium citrinum* cells *hdfA* or *hdfB* (or homologs thereof) genes. The level of knowledge and skill in the art does not allow those skilled in the art to structurally envisage or recognize any or all filamentous fungus, any or all *Aspergillus*, any or all *Penicillium*, any or all *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* having a deletion or mutation of its *hdfA*, *hdfB* or homologs thereof or increased level of a component involved in HR because it is known that corresponding genes in different species tend to differ in sequence and the amount and type of sequence variation is unpredictable. Since the structure of *hdfA*, *hdfB* and homologs thereof would be expected to vary unpredictable from the structure of the *A. niger* and *P. chrysogenum* *hdfA* and *hdfB*, the disclosed *A. niger* and *P. chrysogenum* mutants comprising a deletion of its *hdfA* and *hdfB* do not constitute a representative number of species to describe the whole genus and there is no evidence on the record of the relationship between the structure of the disclosed mutant *A. niger* or *P. chrysogenum* and the structure of any or all filamentous fungus, any or all *Aspergillus*, any or all *Penicillium*, any or all *Trichoderma*, *Aspergillus oryzae*, or *Penicillium citrinum* comprising a deletion or mutation of its *hdfA*, *hdfB* and/or homologs thereof. Because the disclosed *A. niger* and *P. chrysogenum* mutant having a deletion of its *hdfA* and *hdfB* are not representative of the entire claimed genus, and the specification does not disclose structural features shared by members of the genus, the description of the said mutant *A. niger* and *P. chrysogenum* having a deletion of its *hdfA* and *hdfB* would not have put the application in possession of the common structural attributes or features shared by members of the genus that structurally distinguish the members of the genus

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from other materials at the time of filing. Accordingly, the specification does not provide a representative number of species or sufficient common structural features to show that the application would have been in possession of the claimed genus as a whole at the time of filing.

Hence the rejection is maintained.

Other Relevant Art

Ninomiya et al. (reference OR in the IDS filed on September 25, 2006) discloses a filamentous fungus having a mutation of its *KU70* and *KU80* (homologs of *hdfA* and *hdfB*), wherein said mutant has a decreased NHR/HR ratio but is not available as prior art because the reference was published or made known to the public after the instant invention was filed.

Ivanov (US Patent 6,569,681 - reference AR in the IDS filed on September 25, 2006) discloses deleting *KU70* and *KU80* (homologs of *hdfA* and *hdfB*), wherein said mutant has a decreased NHR/HR ratio but is not available as prior art because the reference does not teach a *KU70* and *KU80* (homologs of *hdfA* and *hdfB*) of filamentous fungal cells that prefer NHR over HR.

Conclusion

None of the claims are in condition for allowance.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Yong D Pak/

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Primary Examiner, Art Unit 1652